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# agriculture

## **Report of the Scientific Veterinary Committee, the Scientific Committee for Animal Nutrition and the Scientific Committee for Food on the basis of the report of the scientific group on anabolic agents in animal production**



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EUR 8913 DE, EN, FR, IT



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REPORT OF THE SCIENTIFIC VETERINARY COMMITTEE, SCIENTIFIC COMMITTEE  
FOR ANIMAL NUTRITION AND THE SCIENTIFIC COMMITTEE FOR FOOD ON  
THE BASIS OF THE REPORT OF THE SCIENTIFIC GROUP ON  
ANABOLIC AGENTS IN ANIMAL PRODUCTION

I. INTRODUCTION

On the 31 July 1981 the Council adopted Directive 81/602/EEC<sup>(1)</sup> concerning the prohibition of certain substances having a hormonal action and of any substance having a thyrostatic action.

By Article 5 of that Directive the Council decided to take a decision as soon as possible on the administering to farm animals of oestradiol 17 $\beta$ , testosterone, progesterone, trenbolone and zeranol, for fattening purposes. It also noted the Commissions intention to consult the competent Scientific Committees on the matter.

The Commission asked the Scientific Veterinary Committee, the Scientific Committee for Animal Nutrition and the Scientific Committee for Food the question :

"Does the use for fattening purposes in animals of the following substances : oestradiol - 17 $\beta$ , testosterone, progesterone, trenbolone and zeranol present any harmful effect to health."

To facilitate this work a specific Scientific Group was created in which representatives of each of the Scientific Committees participated.

This document contains the report adopted by the Scientific Group as a result of its final meeting of 22.9.1982. This report was made available to the Scientific Committees whose opinion was requested.

The Scientific Veterinary Committee gave its opinion at its meeting on 9.11.1982.

The Scientific Committee on Animal Nutrition gave its opinion at its 33rd meeting on 17.11.1982.

The Scientific Committee for Food gave its opinion at its 39th meeting on 4.02.1983.

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(1) OJ No L 222 of 07.08.1981, p. 32

## II. REPORT OF THE SCIENTIFIC GROUP ON ANABOLIC AGENTS IN ANIMAL PRODUCTION

### A. COMPOSITION OF THE SCIENTIFIC GROUP

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## B. REPORT

### 1. INTRODUCTION

The Council Directive 81/602/EEC<sup>(1)</sup> concerning the use of certain substances having a hormonal action and of any substances having a thyrostatic action stipulates in Article 5 that the Council would as soon as possible take a decision on the use of oestradiol-17 $\beta$ , progesterone, testosterone, trenbolone and zeranol for the fattening of farm animals. For this purpose the Commission was required to present to the Council, a report on the collected experience and scientific developments in this field. Consequently a Scientific Working Group was set up to advise the Commission of the European Communities on whether the use of oestradiol-17 $\beta$ , testosterone, progesterone, trenbolone and zeranol as anabolic agents in animal production was a risk to public health.

The Terms of Reference of the Scientific Working Group were as follows: -

"Does the use for fattening purposes in animals of the following substances: oestradiol-17 $\beta$ , testosterone, progesterone, trenbolone and zeranol present any harmful effect to health?"

In framing its advice, the Scientific Working Group considered the guidelines prepared by the Scientific Committee for Food<sup>(2)</sup>, the Scientific Committee for Animal Nutrition<sup>(3)</sup> and the Council Directives on Veterinary Medicinal Products (81/851/EEC and 81/852/EEC)<sup>(4)</sup>.

The Working Group decided:

- a) that the most suitable criteria for assessing the safety of anabolic agents (growth promoters) were those set out in Part 2, Chapter I, Section A-D of the Annex of Directive 81/852/EEC of 28 September 1981 on the approximation of laws of the Member States relating to analytical, pharmaco-toxicological and clinical standards and protocols in respect of testing of veterinary medicinal products.
- b) that safety is related to the conditions of use of anabolic agents.

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(1) OJ L 222 of 7. 8.1981, p. 32

(2) Reports of the Scientific Committee for Food (EUR 6892) 10th Series

(3) Reports of the Scientific Committee for Animal Nutrition (1980 EUR 6918)

(4) OJ L 317 of 6.11.1981, p. 1 and 16

The Scientific Working Group gave special consideration to a number of general points, such as the need to protect those segments of the population, e.g. prepubertal children, which were most likely to be affected from the toxicological point of view; the distribution of residues in edible tissues; the conditions of use of anabolic agents for growth promotion and improved feed conversion in relation to the general food supply; the need to avoid illegal use; and the importance of providing sensitive and accurate monitoring procedures on which to base enforcement of compliance with regulations.

Enforcement of proper conditions of use is essential for safeguarding the consumer.

In the opinion of the Scientific Group the appropriate conditions of use include

- a) the site of application should be discardable,
- b) the withholding periods must be observed.

Anabolic sex hormones like oestradiol-17 $\beta$ , testosterone, progesterone, trenbolone and zeranol lead to an increased feed conversion and hence protein deposition in farm animals. The basic mechanisms of action on the molecular level are not completely understood. However, there is increasing evidence that the effects are mediated through the basic hormone-receptor interactions. The food of animals, including man, normally contains natural substances with hormonal activity.

No side effects on animal health have been reported following the recommended use of these materials in growing animals other than those related to their hormonal effects on behavior and the reproductive system. Behavioral problems may occur during the first few weeks following treatment but with careful management these problems are not difficult to overcome. The use of anabolic agents to promote growth in animals intended for breeding is contraindicated because of their adverse effects on the reproductive and endocrine systems.

## 2. PRESENT SITUATION

Based on previous safety evaluations some EEC member states have accepted the use of trenbolone and zeranol and of oestradiol-17 $\beta$ , progesterone and testosterone.



The conditions of use require the drug to be implanted at a site (ear or base of ear) which is discarded at slaughter. Withholding periods have to be observed and doses applied per animal range from 20-40 mg for oestradiol-17 $\beta$  and zeranol, *ca.* 200 mg for progesterone and testosterone and 140-300 mg for trenbolone in the form of its acetate.

Council Directive 81/602/EEC of 31 July 1981 prohibits the placing on the market of stilbenes, stilbene derivatives, their salts and esters and thyrostatic substances for administering to animals of all species.

The Committee did not consider the consequences on the quality of meat of the use of anabolic substances.

### 3. ENDOGENEOUS SEX STEROIDS : OESTRADIOL-17 $\beta$ , TESTOSTERONE AND PROGESTERONE

The Scientific Working Group considered that evaluation of the safety-in-use of oestradiol-17 $\beta$  , testosterone and progesterone included consideration of those derivatives which readily yield the parent compound on hydrolysis after absorption from the site of application.

Physiologically the steroidal sex hormones oestradiol-17 $\beta$  and testosterone as well as the gestagen progesterone control the proper function of the sexual physiology and "anabolism" in man and animals. The sex hormones are secreted by the gonads, the adrenals, and the placenta, the level of secretion being controlled by a complex but well established feedback mechanism. Sex steroids exert their hormonal effects at target tissues by binding to highly specific receptor proteins.

Because these compounds occur naturally they have to be considered as inevitable constituents of food from animal origin. Hormone levels in untreated animals vary widely depending on species, sex and physiological state, eg. adult male cattle produce 40-50 mg testosterone/24 h, cattle in late pregnancy several hundred milligrams of oestrogens/day. Thus the highest tissue levels of androgens are found in the mature male animal and of oestrogens in females during the later stages of pregnancy. Oestradiol-17 $\beta$  , testosterone and progesterone also occur normally in milk in varying amounts depending on the physiological state of the animal. In man and animals endogenous sex hormones are rapidly metabolised predominantly in the

liver to compounds exerting only little, if any, biological activity. A large percentage of these metabolites is excreted directly in the bile following conjugation (glucuronide, sulphate). However, because of systemic circulation, metabolites (both free and conjugated) may be found in the tissues, particularly in the kidney and liver.

Because there is a natural endogenous production of oestradiol-17 $\beta$ , progesterone and testosterone in all farm animals, any residues of these steroids are qualitatively indistinguishable from those derived from the use of these same steroids as anabolic agents administered to animals during life. Under appropriate conditions the treatment of animals with exogenous natural steroids results in residues in edible tissues which are orders of magnitude lower than those that can occur naturally in mature males, females and pregnant females. Therefore in practice no quantitative differences have been observed between treated and untreated animals when the recommended conditions of use were observed. Levels in treated and untreated calves are of the order of 0.1  $\mu$ g testosterone/kg and 0.03  $\mu$ g natural oestrogens/kg edible tissues.

No problems arise concerning contamination of the environment as a result of the administration of endogenous hormones, given the natural background of these substances and their biodegradability.

Levels and production rates of endogenous natural sex hormones vary in humans with age, state of sexual maturity, menstrual cycle and pregnancy. Daily production of oestrogens in infants ranges from 1-40  $\mu$ g, in man from 40-130  $\mu$ g, in women during reproductive life from 50-450  $\mu$ g, in menopausal women from 5-40  $\mu$ g. Daily production of testosterone in infants is about 100  $\mu$ g, in man 4-10 mg, and in women 120-300  $\mu$ g.

In relation to the endogenous sex steroid production in the human, the actual amount of sex steroids consumed with food of animal origin is toxicologically negligible as these steroidal residues do not reach effective concentrations at the relevant hormone receptor sites in target tissues. Moreover, the low oral bioavailability (less than 15 %) of these steroids and the existing tissue barriers in the liver and placenta effectively prevent any adverse toxicological effects from the ingestion of the minute residues of natural sex steroids which may be present in all edible tissues of animals treated with

anabolic hormones. Thus no questions of safety arise in relation to the proper use of oestradiol-17 $\beta$ , progesterone and testosterone in an appropriate form of preparation.

#### 4. EXOGENOUS ANABOLIC AGENTS

##### 4.1. Trenbolone (17- $\beta$ hydroxy trenbolone)

Trenbolone is a synthetic steroid with androgenic activity similar to testosterone but with greater anabolic activity. It has several structural features similar to testosterone but unlike testosterone, it has three conjugated double bonds, and is chemically less stable. The material normally in commerce is trenbolone acetate.

##### Metabolism and Residues

The metabolism of trenbolone acetate has been studied in the rat, calf, heifer, cow and steer. Trenbolone acetate is rapidly hydrolysed to trenbolone, and both trenbolone and its metabolites are rapidly excreted as the glucuronides and sulphates, mostly in the bile. The predominant metabolites identified in the extractable fractions of bile in the rat are trenbolone and a 16-OH and a 17-keto metabolite; while in cattle it is mainly 17 $\alpha$ -hydroxy trenbolone with small amounts of trenbolone and other metabolites. Many of the minor metabolites have been identified in both species. The parent compound and its metabolites have low oral activity.

Following the recommended use of trenbolone acetate in cattle and the application of various methods of assay (radioimmunoassay, thin-layer and high performance liquid chromatography) the main metabolite found in muscle has been shown to be trenbolone (<0.5 ppb muscle) and in liver and kidney a conjugated form at 17 $\alpha$ -hydroxy trenbolone (<3 ppb). 17 $\alpha$ -hydroxy trenbolone has a biological activity at least 10 times less than 17 $\beta$  hydroxy trenbolone.

Similarly following subcutaneous implantation of cattle with trenbolone radiolabelled with tritium, total residues, expressed as trenbolone equivalents, were a few parts per billion ( $10^{-9}$ ) in muscle and approximately 10 times higher in liver and kidney (5-35 ppb). 5-10 % of the total residues labelled with tritium are extractable from meat, liver or kidney, and have been identified as similar to those found in bile. The identity of the remaining

unextractable residues, labelled with tritium, which are most likely irreversible bound, is not known but some tritium is found in the body water. The bioavailability of these unextractable residues in liver, kidney and muscle, following ingestion in rat feeding studies was found to be  $<10\%$ .

Toxicity studies. Acute toxicity studies in several species showed trenbolone to be of low oral toxicity.

In subchronic toxicity studies trenbolone acetate was administered for 8 weeks in the diet of mice without any significant changes apart from those related to hormonal activity, which were still present at 25 mg/kg diet, the lowest level tested. Similar subchronic studies in normal male and female rats and in castrated male rats, extending from 10 days to 3 months, showed increased size of liver, kidney and spleen at high doses and the expected hormonal changes down to dose levels of 50  $\mu\text{g/kg}$  bodyweight. A 14 weeks oral feeding study in pigs produced increased liver weight and liver cell size in females at levels of 2 and 20 mg/kg diet. At the lowest dose level of 100  $\mu\text{g}$  trenbolone acetate/kg diet tested there was no clear absence of a lack of a hormonal effect.

A life-span feeding study in the mouse (dose range 0.5-100 mg/kg diet) extended over about 100 weeks. There was some increase in kidney weight at the highest dose levels in females sacrificed at 13 weeks, an effect typical of androgenic activity. At terminal sacrifice no organ weights were recorded, but there was an increased incidence of liver nodular hyperplasia and tumours in males of all dose groups which reached significance at the two highest dose levels and for females at the highest dose level tested. The control mice also had a high incidence of liver tumours.

Female rats were administered with trenbolone acetate during pregnancy and the pups used in a 112 week feeding study, using doses of 0.5-50 mg/kg diet. A number of mild toxic changes were seen at the highest dose level. A clear cut no-effect level for hormonal activity could not be determined. However, the data indicated that (since the lowest dose group showed no significant changes in all parameters examined compared to controls) a concentration of 0.5 ppm in the diet (25  $\mu\text{g/kg}$  B.W.) is the probable "no-hormonal effect level" for the rat. This result requires confirmation. An increased (though not statistically significant) incidence of pancreatic islet cell tumours

was seen at the highest dose level (50 mg/kg diet). A one-generation reproduction study in rats, using 0.5-16 mg/kg diet in males and 0.5-50 mg/kg diet in females showed a dose related effect on pregnancy rate and litter parameters. No teratogenic effect was seen in two feeding studies in rats. A relay toxicity study has shown that meat from cattle treated at doses 10-25 times greater than the normal doses for  $17\beta$ -oestradiol and trenbolone acetate showed no effects in rats.

Because of the irreversible binding of some residues to macromolecules, which may indicate a genotoxic potential, special attention was given to mutagenicity tests with trenbolone.

Genotoxicity was examined by mutagenicity tests and by the capacity for DNA binding. Neither  $17\beta$ -Trenbolone nor  $17\alpha$ -Trenbolone showed any mutagenic activity in prokaryotic systems nor in any in vivo test for bone marrow and germ cell cytogenetics. Clastogenic activity in vitro against human lymphocytes in culture were negative but tests against cells (L 5178 mouse lymphoma) were slightly positive, but to the same degree shown by testosterone and oestradiol. Concerning DNA binding in vivo in rats covalent binding indices were very low and equivalent for trenbolone and testosterone and less than for oestradiol. The data available to the group do not indicate any genotoxic activity. The question of binding to macromolecules other than DNA is a general problem which the group consider worthy of further study.

The findings of the carcinogenicity studies in rodents are difficult to interpret because of the interference by the hormonal activity of the dose levels employed and the comparatively high incidence of liver tumours in the controls used in the mouse study. The results of the mutagenicity tests do not indicate genotoxic activity. Hence the increased tumour incidence observed at high dose levels is probably due to epigenetic mechanisms related to the modulating effect of the hormonal activity on the mechanism of tumour production. Therefore, further information on the "no hormonal effect" level of trenbolone acetate is necessary.

The present information on the average daily consumption of muscle tissues and offals within the EEC suggest that the consumer would probably be exposed to similar amounts of  $17\alpha$  and  $17\beta$ -hydroxy trenbolone through his food. Therefore more toxicological information

particularly the determination of the no hormone effect level of 17 $\alpha$ -hydroxy trenbolone is desirable. In summary for trenbolone, establishment of the no hormonal effect level of 17- $\beta$  and 17- $\alpha$  trenbolone is required. Clarification is required of carcinogenicity data of 17 $\beta$  trenbolone particularly from the chronic toxicity study by taking into account the mutagenicity studies already completed.

#### 4.2. Zeranol

This substance is structurally not a steroid and does not itself occur in nature although the parent substance zearalenone is a natural substance elaborated by Gibberella Zea. It has oestrogenic and anabolic activity.

##### Metabolism

The metabolism has been studied in a number of species including cattle and sheep. Most of the orally administered substance is absorbed and eliminated in the faeces and urine. The proportions of urinary and faecal elimination is species dependent.

Zeranol is excreted both as free and conjugated substance and as free and conjugated zeralanone. The same metabolites appear in the bile. Most of orally administered zeranol has practically disappeared from the tissues within 24 hours except for the liver and kidney, however, no thorough identification of the possible metabolites has been made in the relevant species.

The oestrogenic properties were studied in many species using comparatively high doses but a no-hormonal effect level has not been determined, activity still being detectable at levels of 30-50  $\mu$ g/animal/day in rats and mice. However, in vitro assays point to zeranol having about 20 % of the oestrogenic activity of oestradiol.

##### Toxicity

Zeranol has a low acute oral toxicity in most species. Subchronic feeding studies for 13 weeks in the rat showed hepatotoxicity in both sexes and none of the doses was free from hormonal activity (lowest dose tested 0.25 mg/kg bodyweight). Feeding studies in dogs ranging from 6-104 weeks and over a wide range of doses showed some haematological effects at high dose levels and evidence of gross hormonal

effects at all levels tested. A no-hormonal effect level was not determined.

A life span feeding study in rats over 2 years at dose levels from 0.8-20 mg/kg bodyweight/day showed hormonal effects in males and females at all dose levels. Some haematological effects at the highest dose levels as well as microscopically detected hepatotoxicity at all levels were noted. No carcinogenic effects were seen.

A seven year study in female beagles showed variable toxic effects at the high dose level on the haemopoietic system with increased weights of liver, kidney and adrenals at all levels but also significant effects due to hormonal activities on all reproductive organs at both dose levels. Female beagles were hysterectomised. Although not specially designed for this purpose, no carcinogenic effects were seen.

A ten year feeding study in female rhesus monkeys using a dose range of 15 and 75 mg/kg bodyweight showed some haematological changes at the highest dose level and alteration in hepatic function at both dose levels tested with increased liver weight at termination. Both dose levels showed significant hormonal effects on the reproductive system, hence a no-hormonal effect level was not determined. Although not specially designed for this purpose, no evidence of carcinogenicity was found.

A three-generation reproduction study in rats combined with a teratology study showed no adverse effects at all levels up to 200 µg/kg diet. Another teratology study in rats showed inhibition of implantation at the lowest dose tested (1 mg/animal/day during 1 to 4 of gestation). A similar study in mice gave no effects on pregnancy and litter parameters at doses below 100 µg/kg bodyweight without showing any teratogenic effects.

Mutagenicity was studied in prokaryotic systems but the toxicity of zeranol for the indicator organism made the study difficult to interpret. Low level exposures in these systems produced no mutagenic effects.

In summary, although a large number of studies have been performed with zeranol, there are insufficient data on the nature of the metabolites, on the quantity and nature of the residues in the

edible tissues of animals and on mutagenicity to interpret the available information in terms of the safety or otherwise of zeranol. A sufficiently sensitive method for determining unlabelled zeranol in edible tissues is not available, although a satisfactory method is available for urine of cattle and sheep. There is not sufficient information about the chemical impurities of the commercial product. None of the experiments permit the establishment of a no-hormonal effect level necessary for the interpretation of the toxicological significance of any residues found in edible tissues of treated animals.

## 5. Conclusions and recommendations

### 5.1.

The Scientific Working Group is of the opinion that the use of oestradiol-17 $\beta$ , testosterone and progesterone and those derivatives which readily yield the parent compound on hydrolysis after absorption from the site of application, would not present any harmful effects to the health of the consumer when used under the appropriate conditions as growth promoters in farm animals.

### 5.2.

Evaluation of the data on "trenbolone" and "zeranol" revealed that some data on the hormonal non-effect-level and the toxicology of these compounds and their metabolites are still missing.

### 5.3.

The Scientific Working Group considers it necessary that additional information be provided before a final conclusion can be given on trenbolone and zeranol.

### 5.4.

Proper programmes to control and monitor the use of anabolic agents are essential.

### 5.5.

It is necessary to continue scientific investigations on the relevance of the present use of the "no-hormone effect" level related to the harmful effects of anabolic agents.



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### III. OPINION OF THE SCIENTIFIC COMMITTEES

#### A. SCIENTIFIC VETERINARY COMMITTEE

##### 1. COMMITTEE MEMBERS :

###### a) Section I : Animal Health

P.H. BOOL	D.J. O'REILLY
M.K. ESKILDSEN	O. PAPADOPOULOS
R. FARINE	V. PAPPARELLA
J. LEUNEN	W. PLOWRIGHT
B. LIESS	GH. SCHLIESSER
J.B. McFERRAN	B. TOMA
C. MEURIER	

###### b) Section II : Public Health

G. CUMONT	CH. LABIE
M. DEBACKERE	G.E. LAMMING
F. KENNY	A. MANDIS
P.S. ELIAS	F. PANEBIANCO
R.J. GILBERT	C. RING
D. GROSSKLAUS	N.P. SKOVGAARD
E.H. KAMPELMACHER	R. VIVIANI

##### 2. OPINION

"The Committee unanimously agreed that it fully supports the conclusions and recommendations of the report of the Commission Scientific Group.

However, the Committee attracted the attention of the Commission to the urgent need for further discussion and action to establish :

- (a) the conditions of use,
- (b) methods of analysis,
- (c) monitoring programmes,

as regards these substances."

## B. SCIENTIFIC COMMITTEE ON ANIMAL NUTRITION

### 1. COMMITTEE MEMBERS :

D.G. ARMSTRONG	H. HEIGENER
G. BALLARINI	S. MALETTO
G. BORIES	B. BREST NEILSEN
P. DORN	M.M. McALEESE
V. ELEZOGLOU	M. VANBELLE
P.S. ELIAS	G.J. VAN ESCH
R. FERRANDO	M. WOODBINE
G. GEDEK	

### 2. OPINION

"The Committee has examined the report by the Commission's scientific working group on anabolic agents used in livestock production and has approved its conclusions and recommendations.

The Committee, however, wishes to draw the Commission's attention to the need to lay down certain essential provisions, in particular as regards the following :

#### a) Instructions for use

1. Specification of the doses, the type of pharmaceutical preparation, the number and frequency of administrations.
2. Association of anabolic agents.
3. Localization of implant and ablation of zone treated.
4. Withdrawal period before slaughter.
5. Identification of animals treated, with indication of the period of treatment.

#### b) Surveillance programme and analysis methods

1. Control of production and trade in anabolic agents.
2. Veterinary control of authorized uses.
3. Means and methods of control."

C. SCIENTIFIC COMMITTEE FOR FOOD

1. COMMITTEE MEMBERS :

P.S. ELIAS	A. POLYCHRONOPOULOU-TRICHOPOULOU
A. HILDEBRANDT	E. POULSEN
F. HILL	J. REY
A.W. HUBBARD	V. SILANO
A. LAFONTAINE	R. TRUHAUT
B. MACGIBBON	G.J. VAN ESCH
A. MARIANI	R. WENNIG
K.J. NETTER	

2. The Committee gave its opinion at its meeting of the 4 February 1983.

Terms of Reference

To give an opinion on whether the use for fattening purposes in animals of the following substances : oestradiol -17 $\beta$ , testosterone, progesterone, trenbolone and zeranol present any harmful effect to health.

Background

On the 31 July 1981 the Council adopted Directive 81/602/EEC<sup>(1)</sup> concerning the prohibition of certain substances having a hormonal action and of any substance having a thyrostatic action.

By Article 5 of that Directive the Council decided to take a decision as soon as possible on the administering to farm animals of oestradiol -17 $\beta$ , testosterone, progesterone, trenbolone and zeranol, for fattening purposes. It also noted the Commission's intention to consult the competent Scientific Committees on the matter.

The Commission asked the Scientific Veterinary Committee, the Scientific Committee for Animal Nutrition and the Scientific Committee for Food the same question, recognizing that the three committees would lay emphasis in their separate reports on the aspects of the question which fell within their terms of reference.

The three Committees established a joint working group composed of members of the committees with special knowledge of the subject.

A number of eminent specialists in the field joined the working group which met several times under the auspices of the Commission Services as a "scientific working group on anabolic agents in animal production".

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(1) OJ No L 222 of 07.08.1981, p. 32

The Scientific Committee for Food, together with the Scientific Committee for Animal Nutrition and Scientific Veterinary Committee, was requested to consider the report of the Scientific Working Group and to comment on its conclusions and recommendations during the Committee's own review.

The committee has been informed that the Commission intends to make public the report of the Scientific Working Group. The Committee also notes that the Scientific Veterinary Committee and the Scientific Committee for Animal Nutrition have both already made recommendations to the Commission on the proper use of these anabolic agents.

#### Current Review

The Committee is impressed by the thoroughness with which the report of the joint working group has been prepared. There appears no reason in the present report to rehearse all the reasoning included therein, particularly in view of its imminent publication.

The conclusions of the Scientific Working Group were as follows :

1. The Scientific Working Group is of the opinion that the use of oestradiol -17 $\beta$ , testosterone and progesterone, and those derivatives which readily yield the parent compound on hydrolysis after absorption from the site of application, would not present any harmful effects to the health of the consumer when used under the appropriate conditions as growth promoters in farm animals.
2. Evaluation of the data on "trenbolone" and "zeranol" revealed that some data on the hormonal no-effect level and the toxicology of these compounds and their metabolites are still missing.
3. The Scientific Working Group considers it necessary that additional information be provided before a final conclusion can be given on trenbolone and zeranol.
4. Proper programmes to control and monitor the use of anabolic agents are essential.
5. It is necessary to continue scientific investigations on the relevance of the present use of the "no-hormone effect" level when related to the harmful effects of anabolic agents.

### Conclusions and Recommendations

In general, the Scientific Committee for Food agrees with the conclusions and recommendations of the Scientific Working Group. It also wishes to put forward the following comments for consideration by the Commission :

- i) In relation to Recommendation 2 it would be of interest to generate data on the threshold values for the toxic and hormonal activities of trenbolone and zeranol.
- ii) The Committee endorses the Recommendation 4 on the importance of implementing programmes for control and monitoring of anabolic agents. It emphasizes that proposals should be made by the Commission for implementation. In connection with this aim it would be necessary to encourage the development and standardisation of appropriate analytical methods.
- iii) The Committee recognises that the possible misuse of naturally occurring hormones or their derivatives, which easily yield the original hormone, may be difficult to detect analytically. Information is therefore needed on the levels of naturally occurring hormones likely to engender a health hazard. It is an important public health consideration to prevent the illegal use of banned products and the misuse of authorised products by efficient monitoring and proper controls.



European Communities — Commission

**EUR 8913 — Report of the Scientific Veterinary Committee, the Scientific Committee for Animal Nutrition and the Scientific Committee for Food on the basis of the report of the scientific group on anabolic agents in animal production**

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By Article 5 of that directive the Council decided to take a decision as soon as possible on the administering to farm animals of oestradiol 17 $\beta$ , testosterone, progesterone, trenbolone and zeranol, for fattening purposes. It also noted the Commission's intention to consult the competent scientific committees on the matter.

The Commission asked the Scientific Veterinary Committee, the Scientific Committee for Animal Nutrition and the Scientific Committee for Food the question: 'Does the use for fattening purposes in animals of the following substances: oestradiol 17 $\beta$ , testosterone, progesterone, trenbolone and zeranol present any harmful effect to health?'

To facilitate this work a specific scientific group was created in which representatives of each of the scientific committees participated.

This document contains the report adopted by the scientific group as a result of its final meeting of 22 September 1982. This report was made available to the scientific committees whose opinion was requested.

The Scientific Veterinary Committee gave its opinion at its 5th meeting on 9 November 1982.

The Scientific Committee on Animal Nutrition gave its opinion at its 33rd meeting on 17 November 1982.

The Scientific Committee for Food gave its opinion at its 39th meeting on 4 February 1983.

<sup>1</sup> OJ L222, 7.8.1981, p.32.



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